IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: **Shellenberger**

Serial No.: **10/663,187**

Group Art Unit: **1617**

Filed: **September 15, 2003**

Examiner: **Hui**

For: **Method of Treating Tremors**

Docket No. 61368-222546 (ZONE-010-U1US)

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Appeal Brief under 37 CFR § 41.37

Appellant is filing this Appeal Brief pursuant to 37 CFR § 41.37.

A Notice of Appeal was filed on February 28, 2006. Appellant respectfully requests that the due date for filing an Appeal Brief be extended one month from April 28, 2006, to May 30, 2006 (the first business day following Sunday, 28 May 2006, and the Federal Holiday on Monday, 29 May 2006). The Commissioner is authorized to charge the one month extension of time fee of **$120** to Deposit Account No. 22-0261. The Commissioner is authorized to charge any other necessary fees or credit any overpayments to Deposit Account No. 22-0261 to maintain the pendency of this Appeal Brief.

The Commissioner is authorized to charge the fee of **$500** pursuant to § 41.20(b)(2) to Deposit Account No. 22-0261. The Commissioner is authorized to charge any other necessary fees or credit any overpayments to Deposit Account No. 22-0261 for consideration of this Appeal Brief.

Accordingly, the Commissioner is authorized to charge the total fee of **$620** to Deposit Account No. 22-0261.

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(i) Real Party in Interest

Eisai, Inc. is the real party in interest by virtue of an assignment recorded on March 24, 2004, at Reel 015133, Frame 0390 from the inventor to Elan Pharmaceuticals, Inc.; and by virtue of an assignment recorded on September 12, 2005, at Reel 016970, Frame 0718 from Elan Pharmaceuticals, Inc. and Elan Pharma International Limited to Eisai, Inc.

(ii) Related Appeals and Interferences

There are no prior and/or pending appeals, interferences or judicial proceedings known to Appellant, the Appellant's legal representative, or the assignee which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(iii) Status of Claims

Claims 1-11 have been canceled from the application.

Claims 12-35 were rejected in the final Office Action dated November 30, 2005, and the Advisory Action dated April 27, 2006.

The rejection of claims 12-35 is being appealed.

(iv) Status of Amendments

No amendments were filed subsequent to the final rejection in the final Office Action dated November 30, 2005.

(v) Summary of Claimed Subject Matter

The claimed subject matter is directed to methods of administering a therapeutically effective amount of a pharmaceutical composition comprising zonisamide to treat tremors. The claimed tremors include essential tremors (i.e., claims 12-20); severe essential tremors in the rest state (i.e., claims 21-28); action tremors (i.e., claims 29-34); and kinetic tremors (i.e., claim 35). *See* Specification at page 4, lines 2-9; 15-31; page 5, lines 1-30; page 6, lines 1-19. Essential tremors include severe essential tremors. *See* Specification at page 4, line 17. Action tremors include drug-induced or toxic tremors, primary orthostatic tremors, dystonic tremors, and neuropathic tremors. *See* Specification at page 5, lines 24-30; page 6, lines 5-19. Appellant has provided clinical data in Example 5 in the specification that shows zonisamide effectively treats tremors in humans. *See* Specification at page 16, lines 5-18.

(vi) Ground of Rejection to be Reviewed on Appeal

The rejection to be reviewed on appeal is whether claims 12-35 lack enablement under 35 U.S.C. § 112, first paragraph.

(vii) Argument

Claims 12-35 satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

On page 2 in the final Office Action dated November 30, 2005, the U.S. Patent and Trademark Office (PTO) rejected the claims as lacking enablement in view of Taira, *No To Shinkei*, 44(1):61-63 (1992) which reports that two patients who were receiving zonisamide for the treatment of epilepsy experienced a side effect of tremors. The PTO indicated that the claims would be rejected "absent evidence to the contrary."

In a response filed February 28, 2006, Appellant directed the PTO's attention to Example 5 in the specification which provided human clinical data showing the efficacy of zonisamide in treating tremors. Example 5 (specification at page 16, lines 5-18) states:

> Zonisamide was used in treatment of patients at an outpatient neurology clinic, which provided the following results. Adverse reactions experienced in treatment were GI upset, somnolence and skin rash. Kidney stones and anhydrosis (lack of sweating) were not encountered in the patients treated. For intractable essential tremor, 10 patients (age range: 46 to 82) were identified who were either intolerant to, or failed on, primidone or propranolol therapy. The dosage of zonisamide to these patients was 100 mg to a maximum of 200 mg once daily. The study dose was continued for at least 12 weeks unless discontinued earlier due to side effects. Of the ten patients, who did not respond to other treatment, four patients responded by reduction in tremor of greater than 50% and reported a better quality of life. Amongst other categories: mixed tremor (non-essential, secondary to trauma or multiple sclerosis), two out of two patients responded; multi-infarct-related (2 or more minor strokes) tremor, one out of two patients responded; and in Parkinsonian tremor, two out of four responded.

Example 5 demonstrates that the claimed methods are enabled because zonisamide was used to successfully treat patients with tremors. Moreover, one skilled in the art could practice the claimed invention without undue experimentation based on Example 5 and other information in the specification (e.g., modes of administration, dosing amounts).

Despite the evidence in the specification demonstrating that the claims are enabled under 35 U.S.C. § 112, first paragraph, the PTO erroneously maintained the rejection for the following reason:

> Applicant's arguments by citing the expamle [sic] 5 in the instant specification have been considered, but are not found persuasive. Examiner did provide evidence that zonisamide can induce tremor. What the instant specification disclosed is a study of zonisamide treating tremor with a specific dose and specific dosing regimen; however, the instant claims are not limited to such dosage range (100 to 200 mg) nor the dosing regimen (continued for at least 12 weeks). Therefore, the 35 USC 112, lack of enablement rejection is maintained.[1]

The PTO provided an article showing that zonisamide caused a side effect of tremors in patients with epilepsy. However, Example 5 in the specification already establishes enablement and successfully rebuts the article about epileptic patients cited by the PTO and demonstrates that the claims are enabled for methods of treating tremors with zonisamide.

The scope of enablement is greater than a specific example. The PTO, however, asserts that the claims must be limited to the specific example in the specification in order to satisfy the enablement requirement. The PTO's position is not supported by Supreme Court case law, Federal Circuit case law, CCPA case law, or the MPEP.

The standard for determining whether the specification meets the enablement requirement was made in the Supreme Court decision of *Mineral Separation v. Hyde,* 242 U.S. 261 (1916) which posed the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988); *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247 (Fed. Cir. 2004); MPEP 2164.01. With

[1] Advisory Action dated April 27, 2006 at page 2.

respect, the PTO is not applying the proper test for enablement in the present application. One skilled in the art could practice the presently claimed methods without undue or unreasonable experimentation in view of the guidance provided by Appellant in Example 5 in the specification, the breadth of the claims, the level of skill in the art, and the routine experimentation needed to practice the claimed invention. Example 5 provides guidance for one skilled in the art to vary the dosage and dosing schedule to determine other therapeutically effective amounts of zonisamide that would be useful for treating tremors or for other dosing schedules that would be effective for treating tremors. This is nothing more than routine experimentation.

The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993); MPEP 2164.08. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. *Chiron Corp. v. Genentech, Inc.* at page 1253. The scope of enablement must only bear a reasonable correlation to the scope of the claims. *In re Fisher*, 427 F.2d 833 (CCPA 1970); MPEP 2164.08.

Claims should not be rejected as being broader than the enabling disclosure under 35 U.S.C. § 112 for not including limitations dealing with factors which would be considered obvious to one of ordinary skill in the art to whom the specification and claims are directed. *In re Skrivan*, 427 F.2d 801 (CCPA 1970) ; MPEP 2164.08. One does not look to the claims but to the specification to find out how to practice the claimed invention. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983); *In re Hyatt*, 708 F.2d 712 (Fed. Cir. 1983); MPEP 2164.08. Limitations and examples in the specification do not generally limit what is

covered by the claims. *Chiron Corp. v. Genentech, Inc.* at page 1253; *In re Goffe*, 542 F.2d 564 (CCPA 1976); MPEP 2164.08.

In the present application, the PTO is asserting that Appellant must limit the claims to the specific dose of zonisamide and specific dosing schedule described in Example 5 in order to satisfy the enablement requirement. The PTO's position is untenable in view of established case law. Example 5 in the specification demonstrates that zonisamide is useful for treating tremors, i.e., the claims are enabled. Again, one skilled in the art could, without undue experimentation, rely on Example 5 as guidance to find other dosages of zonisamide or other dosing schedules that would also be effective for treating tremors. Appellant need not limit the claims to that which is described in Example 5 to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

Appellant respectfully requests that the Board reverse the PTO's rejection under 35 U.S.C. § 112, first paragraph, and direct the Examiner to enter a Notice of Allowance for claims 12-35.

Respectfully submitted,

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Date: May 30, 2006

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(viii) Claims Appendix

12. A method of treating essential tremor in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising zonisamide or a pharmaceutically acceptable salt thereof.

13. The method of claim 12, wherein the essential tremor is severe essential tremor.

14. The method of claim 12, wherein the therapeutically effective amount is in the range of about 0.5 mg/kg/day to about 10 mg/kg/day.

15. The method of claim 12, wherein the pharmaceutical composition is administered orally to the subject.

16. The method of claim 12, wherein the pharmaceutical composition is administered parenterally to the subject.

17. The method of claim 16, wherein the pharmaceutical composition is a sterile solution comprising zonisamide sodium.

18. The method of claim 16, wherein the pharmaceutical composition is administered intravenously, subcutaneously, or intramuscularly.

19. The method of claim 12, further comprising administering another therapeutic agent used to treat essential tremor.

20. The method of claim 12, further comprising administering propranolol, timolol, alprazolam, clonazepam, diazepam, lorazepam, trazadone, mirtazapine, clonidine, a botulinum toxin injection, gabapentin, primidone, phemobarbital or MK-801.

21. A method for treating severe essential tremor in the rest state in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising zonisamide or a pharmaceutically acceptable salt

thereof.

22. The method of claim 21, wherein the therapeutically effective amount is in the range of about 0.5 mg/kg/day to about 10 mg/kg/day.

23. The method of claim 21, wherein the pharmaceutical composition is administered orally to the subject.

24. The method of claim 21, wherein the pharmaceutical composition is administered parenterally to the subject.

25. The method of claim 24, wherein the pharmaceutical composition is a sterile solution comprising zonisamide sodium.

26. The method of claim 24, wherein the pharmaceutical composition is administered intravenously, subcutaneously, or intramuscularly.

27. The method of claim 24, further comprising administering another therapeutic agent used to treat severer essential tremor in the rest state.

28. The method of claim 21, further comprising administering propranolol, timolol, alprazolam, clonazepam, diazepam, lorazepam, trazadone, mirtazapine, clonidine, a botulinum toxin injection, gabapentin, primidone, phemobarbital or MK-801.

29. A method for treating action tremor in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising zonisamide or a pharmaceutically acceptable salt thereof.

30. The method of claim 29, wherein the action tremor is postural tremor.

31. The method of claim 29, wherein the action tremor is drug-induced or toxic tremor; primary orthostatic tremor; dystonic tremor; or neuropathic tremor.

32. The method of claim 29, wherein the action tremor is cerebellar tremor.

33. The method of claim 29, wherein the therapeutically effective amount is in the range of about 0.5 mg/kg/day to about 10 mg/kg/day.

34. The method of claim 29, wherein the pharmaceutical composition is administered orally or parenterally to the subject.

35. A method for treating kinetic tremor in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising zonisamide or a pharmaceutically acceptable salt thereof.

(ix) **Evidence Appendix**

None.

(x) Related Proceedings Appendix

None.